

Serial No. 10/021,425

3196/00/US (26648)

Amendment and response to Office Action dated April 6, 2004 (Amendment B)

June 29, 2004

REMARKS

CLAIM AMENDMENTS

Claims 1, 11, 14 and 57 have been canceled without prejudice. No new claims have been added. Claims 3-9, 30-34, 36-45, 50-56, and 59-77 have been withdrawn from consideration pursuant to a restriction requirement.

Claims 2, 10, 12-13, 15-16, 18, 22, 26, 35, 46-49, and 58 are amended in this Amendment B to improve form and typographical errors. No new matter has been added. The amended claims are supported by the specification and by the claims as originally filed.

Claim 2 is amended to more particularly define the invention. More specifically, claim 2 has been amended from its original form as a claim depending from (canceled) claim 1 to an independent claim. Support for this amendment is found in the originally filed claims 1 and 2.

Claims 10, 12, 13, and 15 are amended to more particularly define the invention. More specifically, claims 10, 12, 13, and 15 have been amended from their original form to define specific substrates of the hydroxylase. Support for this amendment is found in the originally filed claim 10 and Example 20 of the specification.

Claims 46 and 49 are amended to more particularly define the invention.

New claims 78-83 are presented in this Amendment B. Support for these claims is found in the specification on page 6, lines 1-3. Upon entry of this amendment, claims 2, 10, 12-13, 15-29, 35, 46-49, 58, and 78-83 will be pending in the application.

CLAIM REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 46 and 49 stand rejected under 35 U.S.C § 112, second paragraph as indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is respectfully traversed.

As described above, Applicant has amended claims 46 and 49 to improve form and more particularly define the invention. Claim 46 has been amended by removing “any of”. Applicant submits that the amended claim addresses the confusion created by the reference to multiple claims numbered 35. Claim 49 has been amended to more specifically claim the subject matter disclosed in the specification, for example at page 27, lines 11-15 and page 60, lines 20-28 (example 19). Claim 49, part (c) has been amended, with support from the aforementioned sections, to incorporate “fraction microsomes,” which has the effect of providing antecedent basis for the use of the term “fraction microsomes” found in part (d) of the same claim. Claims 46 and 49 as amended particularly point out and distinctly claim the invention. Withdrawal of the rejection is respectfully requested.

CLAIM REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 1, 10-29, 35, 46-49, and 57 stand rejected under 35 U.S.C. §112, first paragraph because the specification does not reasonably provide enablement for claims of the scope of the instant claims. The rejection is respectfully traversed.

The specification teaches the isolation of nucleic acids encoding an *Aspergillus ochraceus* 11 alpha hydroxylase, with the hydroxylase encoded by those nucleic acids able to selectively catalyze the 11 alpha hydroxylation of a genus of steroids without catalyzing the 15 beta hydroxylation of a

subgenus of those steroids. (For selective activity, *see generally* Example 20: page 60, line 29 – page 62, line 19 and Figure 16). The selective activity demonstrated in Example 20 is aligned with that activity shown in Dutta et al. (page 3, lines 27-29).

The Examiner indicates that the teaching of the specification is limited to androstenedione as a suitable substrate for the hydroxylase, rather than the substrates listed in claims 10-15, 18, and 35. In addition to Example 20, in which 11 alpha hydroxylase activity is demonstrated with the androstenedione substrate, *Aspergillus ochraceus* have been used to convert progesterone and other steroids to their corresponding 11 alpha hydroxy forms. (page 2, lines 20-24; page 3, lines 27-29).

Further, Example 20 is illustrative of steroid bioconversions and is not intended to limit the functional range of the 11 alpha hydroxylase. As indicated on page 47, lines 23-25, “ The following examples will illustrate the invention in greater detail, although it will be understood that the invention is not limited to these specific examples.” The presence of Example 20 is demonstrative in nature and intended to show the effect of this hydroxylase, not on a single substrate, but on a class of substrates sharing the same basic polycyclic core. Example 20 provides an assay with which one may determine whether the hydroxylase is active against a particular substrate.

Androstenedione is properly classified as a 3 keto delta 4, 5 steroid. As indicated in the specification, page 8, lines 12-13, a 3 keto delta 4, 5 steroid is also named as a 3 keto delta 4 steroid. One of skill in the art is in the possession of standard steroid carbon numbering schema. (*See e.g.* McMurry, Organic Chemistry, 2nd edition, 1988, pg. 1025). The structure of androstenedione is also known (page 18, line 6). Alternative names include Δ^4 -Androstene-3,17-dione; 17-Ketotestosterone; and, 3,17-Dioxoandrost-4-ene. Each alternative name indicates androstenedione possesses a double bond between carbons 4 and 5, as well as a keto group at carbon 3 – leading to

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the name 3 keto delta 4,5 steroid. Amendments to the claims as discussed, *supra*, are believed to be fully responsive to the Examiner's rejection. Withdrawal of the rejection is respectfully requested.

The Examiner further indicates that one of ordinary skill in the art would not be taught by the instant specification to make and use nucleic acids of the scope of the instant claims without undue experimentation. This rejection is respectfully traversed.

The fact that experimentation is complex does not necessarily make it undue. (MPEP §2164.01). The working examples of the specification, culminating in the data presented in Figure 16, demonstrate in a stepwise fashion, to one of skill in the art, how the invention may be practiced. Amendments to the claims as discussed, *supra*, are believed to be fully responsive to the Examiner's rejection. In consideration of all evidence, a conclusion of enablement may be reached. The specification provides considerable guidance and direction. Withdrawal of the rejection is respectfully requested.

CLAIM REJECTIONS UNDER 35 U.S.C. §102(b)

Claim 57 stands rejected under 35 U.S.C. §102(b) as being anticipated either of Tudzynski, et al. or Kennedy, et al. Claim 57 is canceled in this amendment; thus this rejection has been mooted. Withdrawal of the rejection is respectfully requested.

OBJECTIONS TO CLAIMS

Claims 2 and 58 stand objected as being dependent upon a rejected base claim. These objections are respectfully traversed. As discussed in "Claim Amendments," *supra*, claim 2 has been rewritten in independent form. Claim 58 remains dependent upon claim 2. It is believed that

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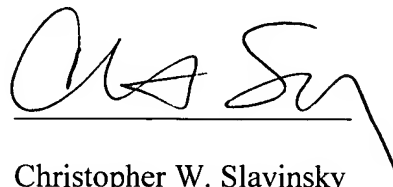
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the amendments to claim 2 place claim 2 in condition for allowance. Withdrawal of the objection is requested.

CONCLUSION

It is believed that all of the stated grounds of rejection and objection have been properly traversed, accommodated or rendered moot by this amendment. It is believed that a full and complete response has been made to the outstanding Office Action, mailed 6 April 2004, and, as such, the present application is in condition for allowance. Thus, prompt and favorable consideration of this amendment is respectfully requested. If the Examiner believes that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (314) 274-7008 at the Examiner's convenience.

Respectfully submitted:

A handwritten signature in black ink, appearing to read 'C. Slavinsky', written over a horizontal line.

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Organic Chemistry

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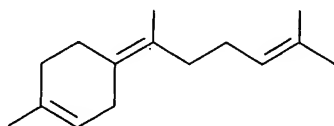
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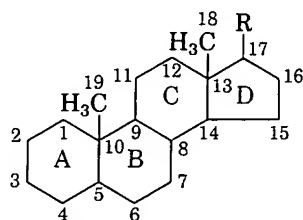
PROBLEM

- 28.8 Propose a plausible pathway to account for the biosynthetic formation of γ -bisabolene from farnesyl pyrophosphate.

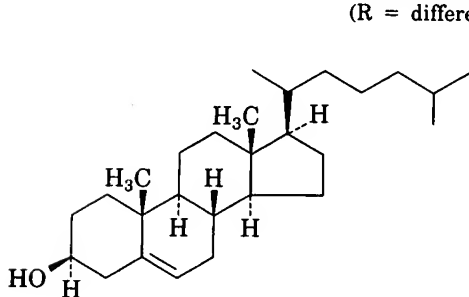
 γ -Bisabolene

28.8 Steroids

In addition to fats, phospholipids, and terpenes, the lipid extracts of plants and animals also contain steroids. A **steroid** is an organic molecule whose structure is based on the tetracyclic ring system shown in Figure 28.8. The four rings are designated A, B, C, and D, beginning at the lower left, and the carbon atoms are numbered beginning in the A ring. Common examples are cholesterol, an animal steroid (and principal component of gallstones), and β -sitosterol, a ubiquitous plant steroid.



Steroid skeleton
(R = different side chains)



Cholesterol (animal sources)

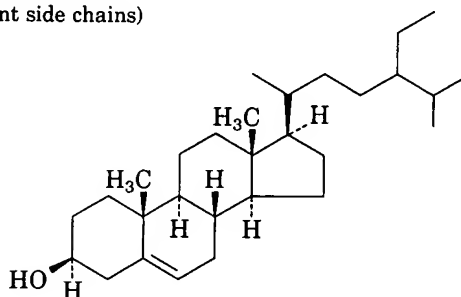
 β -Sitosterol (plant sources)

Figure 28.8 Some representative steroids

Steroids are widespread in both plant and animal kingdoms, and many have useful biological activity. For example, digitoxigenin, a plant steroid found in *Digitalis purpurea* (purple foxglove), is widely used medically as a heart stimulant; androsterone and estradiol are steroid sex hormones; and cortisone is a steroid hormone with anti-inflammatory properties.